WE CLAIM:

1. A method of milling small quantities of one or more candidate compounds comprising:

(a) providing one or more candidate compounds in a liquid dispersion medium in which the candidate compound is poorly soluble;

(b) distributing less than about 15 mL of one or more candidate compound dispersions in at least one compartment of a milling apparatus in the presence of attrition milling media; and

(c) agitating the apparatus such that at least one of the one or more candidate compounds are reduced to an effective average particle size of less than about 2 microns,

wherein at least one surface stabilizer is added to the liquid dispersion medium, either before, during, or after milling.

2. The method of claim 1, wherein the apparatus comprises at least one multiwell plate.

3. The method of claim 2, wherein each well contains a single candidate compound.

4. The method of claim 3, wherein the candidate compound present in each compartment is the same as that present in other compartments of the apparatus, the candidate compound present in each compartment is different from that present in other compartments of the apparatus, or a combination thereof.

5. The method of claim 2, wherein the multiwell plate comprises 2 to 96 wells.

6. The method of claim 5, wherein the multiwell plate comprises 24 to 48 wells.

7. The method of claim 1, wherein the attrition milling media is selected from the group consisting of polymeric media, steel, glass, and ceramic.

8. The method of claim 1, wherein the attrition milling media has a particle size selected from the group consisting of about 3 mm or less, about 2 mm or less, about 1 mm or less, about 500 microns or less, about 400 microns or less, about 300 microns or less, about 200 microns or less, about 100 microns or less, about 50 microns or less, and mixtures thereof.

9. The method of claim 1, wherein the time required for the particle size reduction process is selected from the group consisting of about 10 days or less, about 9 days or less, about 8 days or less, about 7 days or less, about 6 days or less, about 5 days or less, about 4 days or less, about 3 days or less, about 72 hours or less, about 48 hours or less, about 36 hours or less, about 24 hours or less, about 12 hours or less, about 6 hours or less, about 1 hour or less, about 45 minutes or less, about 30 minutes or less, and about 15 minutes or less.

10. The method of claim 1, wherein the dispersion medium is selected from the group consisting of water, aqueous salt solutions, safflower oil,

ethanol, t-butanol, hexane, and glycol.

11. The method of claim 1, wherein the total dispersion volume required for the particle size reduction process is selected from the group consisting of less than about 10 mL, less than about 9 mL, less than about 8 mL less than about 7 mL, less than about 6 mL, less than about 5 mL, less than about 4 mL, less than about 3 mL, less than about 2 mL, less than about 1.75 mL, less than about 1.5 mL, less than about 1.25 mL, less than about 1 mL, less than about 0.75 mL, less than about 0.5 mL, less than about 0.25 mL, or less than about 0.1 mL.

12. The method of claim 1, wherein each of the candidate compounds has a solubility in the liquid dispersion medium selected from the group consisting of less than about 30 mg/ml, less than about 20 mg/ml, less than about 10 mg/ml, less than about 1 mg/ml, and less than about 0.1 mg/ml.

13. The method of claim 1, wherein each of the candidate compounds is in the form of a salt or is conjugated to another substance to render the compound poorly soluble.

14. The method of claim 1, wherein the compounds are reduced to an effective average particle size selected from the group consisting of less than about 1900 nm, less than about 1800 nm, less than about 1700 nm, less than about 1600 nm, less than about 1500 nm, less than about 1400 nm, less than about 1300 nm, less than about 1200 nm, less than about 1100 nm, less than about 1000 nm, less than about 900 nm, less than about 800 nm, less than about 700 nm, less than about 600 nm, less than about 500 nm, less than about 400 nm, less than about 300

nm, less than about 250 nm, less than about 200 nm, less than about 150 nm, less than about 100 nm, less than about 75 nm, or less than about 50 nm.

15. The method of claim 14, wherein at least about 60%, at least about 70%, at least about 80%, at least about 90%, at least about 95%, or at least about 99% of the nanoparticles have a particle size less than the effective average particle size.

16. The method of claim 1, wherein the quantity of candidate compound required for the particle size reduction process selected from the group consisting of less than about 100 mg, less than about 90 mg, less than about 80 mg, less than about 70 mg, less than about 60 mg, less than about 50 mg, less than about 40 mg, less than about 30 mg, less than about 25 mg, less than about 20 mg, less than about 15 mg, less than about 10 mg, less than about 5 mg, less than about 4 mg, less than about 3 mg, less than about 2 mg, less than about 1 mg, less than about 0.75 mg, less than about 0.5 mg, less than about 0.25 mg, less than about 0.1 mg, and less than about 0.05 mg.

17. The method of claim 1, wherein the one or more candidate compounds are independently present in the liquid dispersion medium at a concentration selected from the group consisting of less than about 70%, less than about 60%, less than about 50%, less than about 40%, less than about 30%, less than about 25%, less than about 20%, less than about 15%, less than about 10%, less than about 5%, less than about 4%, less than about 3%, less than about 2%, less than about 1%, less than about 0.5%, less than about 0.1%, less than about 0.01%, and less

than about 0.001%.

18. The method of claim 1, wherein the one or more candidate compounds are independently present in the liquid dispersion medium at a concentration selected from the group consisting of from about 99.99% to about 0.001%, from about 95% to about 0.1%, and from about 90% to about 0.5%, by weight, based on the total combined dry weight of the candidate compound and at least one surface stabilizer, not including other excipients.

19. The method of claim 1, wherein the one or more candidate compounds are selected from the group consisting of a crystalline compound, a semi-crystalline compound, an amorphous compound, a semi-amorphous compound, and a mixture thereof.

20. The method of claim 1, wherein the one or more candidate compounds are selected independently from the group consisting of therapeutic agents, cosmetics, diagnostic agents, agents useful in bioengineering, and agricultural agents.

21. The method of claim 20, wherein the candidate compounds are agricultural agents selected from the group consisting of pesticides, fertilizers, insecticides, and herbicides.

22. The method of claim 1, wherein at least one candidate compound is selected from the group consisting of COX-2 inhibitors, anticancer agents, NSAIDS, proteins, peptides, nutraceuticals, anti-obesity agents, corticosteroids, elastase inhibitors, analgesics, anti-fungals, oncology therapies, anti-emetics, analgesics, cardiovascular agents, anti-

inflammatory agents, anthelmintics, anti-arrhythmic agents, antibiotics, anticoagulants, antidepressants, antidiabetic agents, antiepileptics, antihistamines, antihypertensive agents, antimuscarinic agents, antimycobacterial agents, antineoplastic agents, immunosuppressants, antithyroid agents, antiviral agents, anxiolytics, sedatives, astringents, beta-adrenoceptor blocking agents, blood products and substitutes, cardiac inotropic agents, contrast media, cough suppressants, diagnostic agents, diagnostic imaging agents, diuretics, dopaminergics, haemostatics, immunological agents, lipid regulating agents, muscle relaxants, parasympathomimetics, parathyroid calcitonin and biphosphonates, prostaglandins, radio-pharmaceuticals, sex hormones, anti-allergic agents, stimulants and anoretics, sympathomimetics, thyroid agents, vasodilators, xanthines, acne medication, alpha-hydroxy formulations, cystic-fibrosis therapies, asthma therapies, emphysema therapies, respiratory distress syndrome therapies, chronic bronchitis therapies, chronic obstructive pulmonary disease therapies, organ-transplant rejection therapies, therapies for tuberculosis and other infections of the lung, and respiratory illness therapies associated with acquired immune deficiency syndrome.

23. The method of claim 22, wherein the nutraceutical is selected from the group consisting of dietary supplements, vitamins, minerals, herbs, healing foods that have medical or pharmaceutical effects on the body, folic acid, fatty acids, fruit and vegetable extracts, vitamin supplements, mineral supplements, phosphatidylserine, lipoic acid, melatonin, glucosamine/chondroitin, Aloe Vera, Guggul, glutamine, amino acids, green tea, lycopene, whole foods, food additives, herbs, phytonutrients, antioxidants, flavonoid constituents of fruits, evening primrose oil, flax

seeds, fish and marine animal oils, and probiotics.

24. The method of claim 1, wherein the at least one surface stabilizer is independently present in an amount selected from the group consisting of from about 0.01% to about 99.999%, about 5% to about 99.9%, and about 10% to about 99.5%, by weight, based on the total dry weight of the candidate compound and surface stabilizer, not including other excipients.

25. The method of claim 1, wherein at least two surface stabilizers are added to at least one candidate compound, either before or after milling.

26. The method of claim 1, wherein the at least one surface stabilizer is selected from the group consisting of a nonionic surface stabilizer, an anionic surface stabilizer, a cationic surface stabilizer, and an ionic surface stabilizer.

27. The method of claim 26, wherein the at least one surface stabilizer is selected from the group consisting of cetyl pyridinium chloride, gelatin, casein, phosphatides, dextran, glycerol, gum acacia, cholesterol, tragacanth, stearic acid, stearic acid esters and salts, calcium stearate, glycerol monostearate, cetostearyl alcohol, cetomacrogol emulsifying wax, sorbitan esters, polyoxyethylene alkyl ethers, polyoxyethylene castor oil derivatives, polyoxyethylene sorbitan fatty acid esters, polyethylene glycols, dodecyl trimethyl ammonium bromide, polyoxyethylene stearates, colloidal silicon dioxide, phosphates, sodium dodecylsulfate, carboxymethylcellulose calcium, hydroxypropyl celluloses, hydroxypropyl methylcellulose, carboxymethylcellulose sodium, methylcellulose, hydroxyethylcellulose, hydroxypropylmethyl-cellulose

phthalate, noncrystalline cellulose, magnesium aluminum silicate, triethanolamine, polyvinyl alcohol, polyvinylpyrrolidone, 4-(1,1,3,3-tetramethylbutyl)-phenol polymer with ethylene oxide and formaldehyde, poloxamers, poloxamines, a charged phospholipid, dimyristoyl phophatidyl glycerol, dioctylsulfosuccinate, dialkylesters of sodium sulfosuccinic acid, sodium lauryl sulfate, alkyl aryl polyether sulfonates, mixtures of sucrose stearate and sucrose distearate, triblock copolymers of the structure: -(-PEO)--(-PBO-)--(-PEO-)-, p-isononylphenoxypoly-(glycidol), decanoyl-N-methylglucamide; n-decyl β-D-glucopyranoside, n-decyl β-D-maltopyranoside, n-dodecyl β-D-glucopyranoside, n-dodecyl β-D-maltoside, heptanoyl-N-methylglucamide, n-heptyl-β-D-glucopyranoside, n-heptyl β-D-thioglucoside, n-hexyl β-D-glucopyranoside, nonanoyl-N-methylglucamide, n-noyl β-D-glucopyranoside, octanoyl-N-methylglucamide, n-octyl-β-D-glucopyranoside, octyl β-D-thioglucopyranoside, lysozyme, a PEG derivatized phospholipid, PEG derivatized cholesterol, a PEG derivatized cholesterol derivative, PEG derivatized vitamin A, PEG derivatized vitamin E, and random copolymers of vinyl acetate and vinyl pyrrolidone.

28. The method of claim 26, wherein at least one cationic surface stabilizer is selected from the group consisting of a polymer, a biopolymer, a polysaccharide, a cellulosic, an alginate, a nonpolymeric compound, and a phospholipid.

29. The method of claim 26, wherein the at least one surface stabilizer is selected from the group consisting of cationic lipids, benzalkonium chloride, sulfonium compounds, phosphonium compounds, quarternary ammonium compounds, benzyl-di(2-chloroethyl)ethylammonium bromide, coconut trimethyl ammonium chloride, coconut trimethyl ammonium

bromide, coconut methyl dihydroxyethyl ammonium chloride, coconut methyl dihydroxyethyl ammonium bromide, decyl triethyl ammonium chloride, decyl dimethyl hydroxyethyl ammonium chloride, decyl dimethyl hydroxyethyl ammonium chloride bromide, C_{12-15}dimethyl hydroxyethyl ammonium chloride, C_{12-15}dimethyl hydroxyethyl ammonium chloride bromide, coconut dimethyl hydroxyethyl ammonium chloride, coconut dimethyl hydroxyethyl ammonium bromide, myristyl trimethyl ammonium methyl sulphate, lauryl dimethyl benzyl ammonium chloride, lauryl dimethyl benzyl ammonium bromide, lauryl dimethyl (ethenoxy)$_4$ ammonium chloride, lauryl dimethyl (ethenoxy)$_4$ ammonium bromide, N-alkyl (C_{12-18})dimethylbenzyl ammonium chloride, N-alkyl (C_{14-18})dimethyl-benzyl ammonium chloride, N-tetradecylidmethylbenzyl ammonium chloride monohydrate, dimethyl didecyl ammonium chloride, N-alkyl and (C_{12-14}) dimethyl 1-napthylmethyl ammonium chloride, trimethylammonium halide, alkyl-trimethylammonium salts, dialkyl-dimethylammonium salts, lauryl trimethyl ammonium chloride, ethoxylated alkyamidoalkyldialkylammonium salt, an ethoxylated trialkyl ammonium salt, dialkylbenzene dialkylammonium chloride, N-didecyldimethyl ammonium chloride, N-tetradecyldimethylbenzyl ammonium, chloride monohydrate, N-alkyl(C_{12-14}) dimethyl 1-naphthylmethyl ammonium chloride, dodecyldimethylbenzyl ammonium chloride, dialkyl benzenealkyl ammonium chloride, lauryl trimethyl ammonium chloride, alkylbenzyl methyl ammonium chloride, alkyl benzyl dimethyl ammonium bromide, C_{12} trimethyl ammonium bromides, C_{15} trimethyl ammonium bromides, C_{17} trimethyl ammonium bromides, dodecylbenzyl triethyl ammonium chloride, poly-diallyldimethylammonium chloride (DADMAC), dimethyl ammonium chlorides, alkyldimethylammonium halogenides, tricetyl methyl ammonium chloride, decyltrimethylammonium bromide, dodecyltriethylammonium bromide, tetradecyltrimethylammonium bromide, methyl

trioctylammonium chloride, POLYQUAT 10™, tetrabutylammonium bromide, benzyl trimethylammonium bromide, choline esters, benzalkonium chloride, stearalkonium chloride compounds, cetyl pyridinium bromide, cetyl pyridinium chloride, halide salts of quaternized polyoxyethylalkylamines, MIRAPOL™, ALKAQUAT™, alkyl pyridinium salts; amines, amine salts, amine oxides, imide azolinium salts, protonated quaternary acrylamides, methylated quaternary polymers, cationic guar, polymethylmethacrylate trimethylammonium bromide, polyvinylpyrrolidone-2-dimethylaminoethyl methacrylate dimethyl sulfate, hexadecyltrimethyl ammonium bromide, poly (2-methacryloxyethyltrimethylammonium bromide) (S1001), poly(N-vinylpyrrolidone/2-dimethylaminoethyl methacrylate) di methylsulphate quarternary (S1002), and poly(2-methylacryloxyamidopropyltrimethylammonium chloride) (S1004).

30. The method of claim 1, wherein:

(a) the one or more candidate compounds are provided in a solvent in which the candidate compounds are dissolved;

(b) the dissolved candidate compounds are distributed into one or more compartments of a milling apparatus;

(c) the solvent is evaporated;

(d) water or a surface stabilizer solution is added to the compartments of the milling apparatus; and

(e) agitating the milling apparatus such that at least one of the one or more candidate compounds are reduced to an effective average particle size of less than about 2 microns.

31. A high throughput screening method comprising:

(a) providing one or more candidate compounds in a liquid dispersion medium in which the candidate compound is poorly soluble;

(b) distributing less than about 15 mL of one or more candidate compound dispersions in at least one compartment of a milling apparatus in the presence of attrition milling media; and

(c) agitating the apparatus such that at least one of the one or more candidate compounds are reduced to an effective average particle size of less than about 2 microns, wherein at least one surface stabilizer is added to the liquid dispersion medium in each well comprising candidate compound, either before, during, or after milling; and

(d) screening the candidate compounds obtained in step (c) in a conventional high throughput screening assay to determine if one or more of the candidate compounds exhibits a desired activity.

32. The method of claim 31, wherein the high throughput screening assay is an enzymatic or whole cell assay.

33. The method of claim 31, wherein the one or more milled candidate compounds obtained in (c) are used directly in the high throughput screening assay in (d).

34. The method of claim 31, wherein the high throughput screening assay is automatic.

35. The method of claim 31, wherein a mixture of two or more candidate compounds is screened in (c).

36. The method of claim 31, wherein

(a) the one or more candidate compounds are provided in a solvent in which the candidate compounds are dissolved;

(b) the dissolved candidate compounds are distributed into one or more compartments of a milling apparatus;

(c) the solvent is evaporated;

(d) water or a surface stabilizer solution is added to the compartments of the milling apparatus; and

(e) agitating the milling apparatus such that at least one of the one or more candidate compounds are reduced to an effective average particle size of less than about 2 microns.

37. A high throughput screening method comprising:

(a) screening one or more candidate compounds in a conventional high throughput screening assay to determine if one or more of the candidate compounds exhibit a desired activity;

(b) formulating the one or more candidate compounds exhibiting a desired activity into a dispersion in which the one or more candidate compounds are poorly soluble;

(c) distributing less than about 15 mL of one or more candidate compound dispersions in at least one compartment of a milling apparatus in the presence of attrition milling media; and

(d) agitating the apparatus such that at least one of the one or more candidate compounds are reduced to an effective

average particle size of less than about 2 microns, wherein at least one surface stabilizer is added to the liquid dispersion medium in each well comprising candidate compound, either before, during, or after milling; and

(e) determining if the one or more candidate compounds exhibiting the desired activity have acceptable solubility, dispersibility, or a combination thereof.

38. The method of claim 37, wherein the high throughput screening assay is an enzymatic or whole cell assay.

39. The method of claim 37, wherein the high throughput screening assay is automatic.

40. The method of claim 37, wherein a mixture of two or more candidate compounds is screened in (a).

41. The method of claim 37, wherein:

(a) the one or more candidate compounds are provided in a solvent in which the candidate compounds are dissolved;

(b) the dissolved candidate compounds are distributed into one or more compartments of a milling apparatus;

(c) the solvent is evaporated;

(d) water or a surface stabilizer solution is added to the compartments of the milling apparatus; and

(e) agitating the milling apparatus such that at least one of the one or more candidate compounds are reduced to an effective average particle size of less than about 2 microns.